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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/520,901

04/13/2005

Toshiyoshi Fujiwara

09857/0202272-US0

2780

7278

7590

02/29/2008

DARBY & DARBY P.C.

P.O. BOX 770

Church Street Station

New York, NY 10008-0770

EXAMINER

SHEN, WU CHENG WINSTON

ART UNIT

PAPER NUMBER

1632

MAIL DATE

DELIVERY MODE

02/29/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	Application No. 10/520,901	Applicant(s) FUJIWARA ET AL.	
	Examiner WU-CHENG Winston SHEN	Art Unit 1632	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 14 January 2008 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
- b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
- (a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ They raise the issue of new matter (see NOTE below);
- (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: See Continuation Sheet. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
- The status of the claim(s) is (or will be) as follows:
- Claim(s) allowed: _____.
- Claim(s) objected to: _____.
- Claim(s) rejected: 4-11.
- Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/Valarie Bertoglio/
 Primary Examiner
 Art Unit 1632

Continuation of 3. NOTE: Independent claim 4 is proposed to be amended to read as follows: A polynucleotide cassette comprising an hTERT promoter operably linked with an E1A gene, an IRES sequence, and an E1B gene in this order, wherein the cassette is capable of replicating in a cancer cell. The proposed amendments "wherein the cassette is capable of replicating in a cancer cell" raise new issues that would require further consideration and/or search in terms of 112 first issues because independent claim 4 recites a polynucleotide cassette, which may not be capable of replicating in a cancer cell as a recombinant virus recited in dependent claim 4.

Continuation of 11. does NOT place the application in condition for allowance because:

Applicant's arguments have failed to overcome the scope of enablement rejection of claims 4-11 under 35 U.S.C. 112, first paragraph, because Applicant's arguments have been fully considered, and found not persuasive. As discussed in the Final office action dated 11/20/2007, pages 6-10, Example 6 does not provide any in vivo evidence and/or arguments that the anticancer activity on the transplanted human lung cancer cell H1358 in nude mice after administration of the claimed polynucleotide cassette. To the best of the Examiner's understanding of Applicant's arguments, Example 6 demonstrates that administration of TRAD vector bearing an insertion of claimed cassette can kill human cancer cell transplanted in a mouse and in the same experimental setting administration of Ad-p53 vector can kill cancer cells by expressing therapeutic gene p53. It appears that Ad-p53 in Example 6 serves as a positive control in term of killing cancer cell. In this regard, the Examiner notes that Example 6 misses a negative control with the same TRAD vector but without an insertion of claimed polynucleotide cassette to conclude that the cancer killing effect is attributed to the expression of claimed polynucleotide cassette. In light of lack of support of claimed invention pertaining to the in vivo cancer cell killing effect asserted by instant application, Applicant's arguments that in vivo testing is not necessary to satisfy the "how to use" of 112 first enablement requirement, are found not persuasive. The Examiner further notes that the citation of In re Brana pertaining to the effect of a given chemical compound for treatment of cancer is unrelated to approach, broadly encompassed by gene expression/therapy, taken by instant application. The rejection is maintained of the record.

Applicant's arguments have failed to overcome the rejection of claims 4-8 and 11 under 35 U.S.C. 103(a) as being unpatentable over Morin et al., taken with Li et al. because Applicant's arguments have been fully considered, and found not persuasive. Applicant's arguments focus on that there would have been no motivation to alter the teachings of Morin and Li to arrive at the claimed invention and no likelihood of success for killing. The essence of Applicant's arguments are essentially the same as the arguments Applicant responded to Non-Final office action. In this regard, The Examiner has addressed Applicant's arguments in the Final office action dated 11/20/2007, pages 15-17. It is worth repeating that the arguments Li et al demonstrated the oncolytic adenovirus in liver cancer only, which is different from the claimed invention that can be utilized in a variety cancers, as Applicant has asserted, are found not persuasive. The Examiner notes that a liver cancer is a species of cancer encompassed by the listed genus of cancers in claim 9 of instant application. The claimed invention broadly reads on liver cancer taught by Li et al. The only new ground of arguments Applicant provides in the response after Final office action is the citation of Mizuguchi et al., Molecular therapy, 1(4) (April 2002), which teaches that IRES-dependent second gene expression is less efficient than cap-dependent first gene expression. In response, the Examiner notes that Mizuguchi et al. only provides a general statement regarding the relative expression levels of gene under IRES translational control. There is no specific teachings in Mizuguchi et al. that are relevant to the claimed polynucleotide cassette of instant application in term of whether the expression of E1A and E1B has to be at the same level from the claimed cassette to arrive at the claimed cancer cell killing effect of the polynucleotide cassette, when administered. The rejection is maintained of the record..